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FIBROMYOMA OF THE UTERUS COMPLICATED BY CANCER OR SARCOMA

WITH REPORT OF THIRTY-FIVE CASES

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The careful study of fibroid tumors of the uterus in the last few years has shown that these tumors are not the benign innocuous growths they were once believed to be. Each succeeding series studied shows more clearly that the dangers of these growths are not only from the symptoms produced by the tumors themselves, such as hemorrhage. etc., but also from the complications and degenerations incident to their continued presence in the uterus.

The most important change or complication which may occur in these fibroid growths is their association with malignant changes either in the tumor itself or in its host, the uterus. This malignant change or association has a very direct bearing on the treatment of these tumors in that, if it can be proved that there is a large percentage of malignancy in the growths or dependent on their presence in the uterus, a weighty argument has been made in favor of early operation and removal.

This malignant complication may occur in two ways, either as a direct degeneration in the tumor itself, as in sarcomatous degeneration. or as an association of cancerous or sarcomatous disease in a uterus already the host of a fibroid tumor.

It is difficult in some cases to decide whether a fibroid tumor has previously existed in a uterus which is now the seat of extensive malignant disease, for the destructive malignant lesion may have caused a disappearance of the fibroid growth or the growth itself may have created tumor formation to simulate the necrotic remains of a fibroid. This is particularly true of sarcomatous disease, and the small percentage (1 per cent.) of sarcomatous degeneration in this series compared with others is held to be due to the fact that no tumor was included in this series unless it was distinctly shown that there was a true sarcomatous degeneration.

The association of malignant change with fibromyomata has had renewed study since my paper[1] in 1904, where, in a series of 280 cases of fibromyomata, it was shown that there was a considerable percentage of malignant changes; three cases of sarcomatous degeneration were reported, with one case of chorioepithelioma. These four cases are included in the present series of thirty-five cases of fibroid tumors complicated by malignant disease, cancer, sarcoma or chorioepithelioma malignum. These cases have been placed in three tables. Table 1 shows the percentage of occurrence of cancer in fibroid disease in a series of 700 routine cases; Table 2

TABLE 1.—CANCER ASSOCIATED WITH FIBROIDS

Age.	Total Fibroids.	Adenocarcinoma of Fundus.		Squamous Carcinoma of Cervix.	
		No.	%	No.	%
20-30	19	0	0		
30-40	233	0	0	1	0.4
40-50	332	12	3.6	1	0.3
50-60	95	6	6.3	3	3
60-70	21	2	9.5	1	4.6
	700	20	2.9	6	0.8

TABLE 2.—SARCOMA AND CHORIOEPITHELIOMA ASSOCIATED WITH FIBROIDS

Age.	Total Fibroids.	Sarcoma.		Chorioepithelioma.	
		No.	%	No.	%
20-30	19	0			0
30-40	233	0			0
40-50	332	2	0.6	2	0.6
50-60	95	3	3		
60-70	21	2	9.5		0
	700	7	1	2	0.3

TABLE 3.—TOTAL MALIGNANT COMPLICATIONS

Age.	Total Fibroids.	Malignancy.	
		No.	%
20-30	19		
30 40	233	1	0.4
40-50	332	17	5
50-60	95	12	12.7
60-70	21	5	23.8
	700	35	5

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[1] McDonald, Ellice: Complications and Degenerations of Uterine Fibromyomata, THE JOURNAL, 1904, May 21, xlii, 1344.

contains the complications of sarcoma and chorioepithelioma and their relation to 700 fibroid tumors, while Table 3 is a summary of the previous two and gives the total percentage of occurrence of malignancy in the 700 tumors. These 700 cases[2] include the series of 280 studied in my previous paper of 1904.

It is also of importance as bearing on the treatment of these growths to know not only the percentage of occurrence of malignant change, but the age at which such change is likely to take place. For this reason the age of the patient at the time of operation has been included in the tables and the percentage of occurrence of each form of malignancy at each decade is shown.

CANCER AND FIBROID TUMORS

While the frequent association of cancer with fibroid tumors has been recognized for many years, it is only since more exact methods of examination have been introduced that adenocarcinoma of the fundus was found to be a much more frequent association than was squamous carcinoma of the cervix.

It was noted in my paper of 1904 that "it seems at least that, while the association of squamous carcinoma with fibroids is accidental, the occurrence of adenocarcinoma may be more or less influenced by the presence of fibroid tumors." This statement has been borne out by many investigators, notably Piquand,[3] who has collected 179 cases of this association and has reported three cases of his own. Isolated cases, however, have little value or bearing on the treatment, for it must be proved that the liability to cancer is of sufficient importance to constitute an indication for the routine removal of these growths, and to do this not only must the total number of cases be noted but the varying percentage of the forms of cancer and the age at which they occur.

Noble[4] has collected from the various reports 4,880 cases of fibroid tumors, which showed cancer of the cervix as a complication in 63 cases and cancer of the body of the uterus in 75 cases.

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[2] These cases are from the records of the Bender laboratory, and I am indebted to Dr. Wolbach, the director, for access to the later ones.

[3] Piquand: Ann. de gyn., July and August, 1905, new series, ii.

[4] Noble, Charles P.: Fibroid Tumors of the Uterus, THE JOURNAL A. M. A., 1906, xlvii, 1881, 1998, 2065.

From the foregoing collection it may be seen that, while the age is not noted, adenocarcinoma occurs as a complication of fibroids in 1.5 per cent. and squamous carcinoma in 1.3 per cent. In the cases reported in this paper adenocarcinoma occurred in 2.9 per cent. and squamous carcinoma in 0.8 per cent.; in other words, there were three times as many cases of adenocarcinoma as there were of squamous carcinoma.

This proportion is entirely the reverse of the usual proportional occurrence, as is shown by Piquand's collection of 1,135 cases of uterine cancer, in which he found 100 cases of squamous carcinoma to 17 cases of adenocarcinoma; and also from the records of the Johns Hopkins Hospital,[*] where there were found 412 cases of squamous carcinoma and 78 cases of adenocarcinoma, a proportion of 100 to 18.

It is obvious, therefore, that adenocarcinoma is relatively more frequent in association with fibroid tumors than is squamous carcinoma. This relationship may result from a common etiologic factor, or the fibroids may predispose toward the occurrence of adenocarcinoma of the fundus.

The fact that myoma of the uterus, as is well known, predisposes toward sterility, and that squamous carcinoma is found but seldom in women who have never had children, may have something to do with the apparent frequency of adenocarcinoma: in other words, women who have fibroids have no children and so are not likely to have squamous carcinoma of the cervix.

Although this may seem apparent, the argument on investigation develops several flaws. First of all, the percentage of sterility has been estimated by gynecologists on operative cases, as is shown by the proportion of sterility given by Mann,[5] 64 per cent.; Frederick,[6] 52.8 per cent.; Giles,[7] 60 per cent., and Cullen,[8] 52 per cent. It is obvious that if the percentage of 14.8 of occurrence of fibroids is correct, as shown by my autopsies reported in 1904, so that one woman in seven has a fibroid tumor, many women who never see a gynecologist have fibroids. Hence a gynecologist's percentage of sterility is not exact, but the actual percentage of sterility is probably lower.

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[*] Sampson, John A.: Importance of an Early Diagnosis in Cancer of the Uterus, THE JOURNAL A. M. A., 1905, xliv, 1586.

[5] Mann: Am. Jour. Obst., June, 1907.

[6] Frederick: Am. Gynec., 1902, i.

[7] Giles: Lancet, London, March 2, 1907.

[8] Cullen: Cancer of the Uterus, 1900.

It may be that the common etiologic factor is in the uterus itself and that there is some quality in the organ which makes it liable to become the seat of fibroid and malignant disease. This, however, is at present impossible of proof.

While a common etiologic factor may explain in part the association of adenocarcinoma and fibroid tumors, it is probable that the fibroid has some part in the frequency of this association. It has been suggested that the irritation of the fibroid tumor may cause congestion of the mucous membrane, alteration in the blood supply, and hyperplasia of the endometrium. Against this theory, however, it may be said that fibroids, unless they are sloughing, cause as a rule very little visible alteration in the mucous membrane, and it is held that there is usually a preliminary hyperplasia of the endometrium before adenocarcinoma occurs.

Mechanical disturbance of the circulation may be a factor. Of 20 cases here reported, calcification was present in 6 of the fibroids and necrosis in 4 cases. In 15 of the cases the fibroids were multiple and in 5 single. As may be seen from the table, no case of adenocarcinoma occurred in a patient under 40 years of age, and the percentage of occurrence increased with each decade.

In squamous carcinoma there was but one of the six cases in a patient less than 40 years of age, and the percentage of occurrence increased with each decade.

While fibroids may bear a causal relation to or have a common cause with adenocarcinoma, the association of squamous carcinoma is accidental. And, while the etiologic relation of the combination of adenocarcinoma with fibroids is obscure, the fact of the large percentage of this complication remains to be taken into account in regard to the treatment of these growths.

SARCOMATOUS DEGENERATION

There were seven cases of sarcomatous degeneration among 700 fibroid tumors. During the time the seven cases of malignant degeneration were observed there were twelve other cases of sarcoma of the uterus.

The tendency of pathologists in the past has been to doubt the possibility of a sarcoma arising from a myoma of the uterus, but most now admit its possibility. So good an observer as Mallory[9] states that he has studied a tumor, which without doubt was a malignant leiomyoma, and in which "the tumor cells tend to differentiate into perfect muscle cells." Such a possibility has long been recognized by gynecologists.

Tracy's[10] collection of 3,561 cases of fibroids gives 54 cases (1.5 per cent.) of sarcomatous degeneration. This form of malignancy is the one most frequently overlooked, as is shown by Winter's[11] two series. In the first of 500 cases only the suspicious points were examined microscopically, and sarcomatous degeneration was found in 3.2 per cent. In the second series of 253 cases in which sections were taken systematically sarcoma was found in 4.3 per cent. Winter believes that if myomata were examined systematically sarcoma would be found in about 4 per cent. of all cases. But this view is not borne out by this series, in which microscopic examination was made of all tumors.

The frequency of this degeneration will be seen from Table 2 to increase with each decade, being 0.6 per cent. in the fourth, 3 per cent. in the fifth and 9.5 per cent. in the sixth. No instance of this degeneration occurred before 40 years of age.

CHORIOEPITHELIOMA MALIGNUM

There were two instances of this complication, both of which occurred in the fourth decade. Both occurred after abortion, and one infiltrated the substance of the fibroid tumor, as was reported in my paper of 1904.

These two cases are supposed to be the only two instances reported of this association of chorioepithelioma malignum and fibroid tumor. Noble[12] reported one case, which, however, was afterward held by his pathologist, Babcock, to be a chorioepithelioma alone. The latter states: "In the early description of the growth it was described as a sarcomatous or endotheliomatous degeneration of a fibroid tumor, but restaining gives no evidence that fibromuscular tissue is present more than would accompany the growth of the syncytial tumor. It is believed that this is a primary syncytioma malignum in a uterus not the seat of any other tumor."

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[9] Mallory: Buck's Reference Handbook of the Medical Sciences (Sarcoma).

[10] Tracy, S. E.: Fibromyomata, Degenerations, Complications and Associated Conditions, Surg., Gynec. and Obst., 1908, vi, 246.

[11] Winter: Zeitschr. f. Geb. u. Gynäk., 1906, vol. vii, 1.

[12] Am. Jour. Obst., 1898, xlvi, 3.

The complication is a rare one and is mostly of interest because of its rarity.

TOTAL MALIGNANT COMPLICATIONS

The total number and percentage of malignant complications of 700 fibroid tumors, then, were 35 cases (5 per cent.), including 20 of adenocarcinoma, 6 of squamous carcinoma, 7 of sarcoma and 2 of chorioepithelioma malignum. Of these 35 cases, 27 cases (those of adenocarcinoma and sarcoma) were due to or influenced by the presence of the fibroid tumor, while 8 cases (those of squamous carcinoma and chorioepithelioma malignum) were of accidental association, that is, their occurrence was not influenced by the presence of fibroid tumor.

There was but one case of malignant complication, a squamous carcinoma, in a patient below 40 years of age; with each decade after 40 the percentage of malignancy increased markedly, being 5 per cent. in the fifth, 12.7 per cent. in the sixth, and 23.8 per cent. in the seventh.

In view of this large percentage of occurrence of fatal disease among patients having fibroid tumors, and the great increase of malignant complications after 40 years of age, it seems wise that a physician should advise all patients who have fibroid tumors and are over 40 years of age, to have these growths removed; for, if the fibroid is not removed, the probabilities are that malignant change will result in one case in every twenty between the ages of 40 and 50, one case in every eight between the ages of 50 and 60 and one case in every four between the ages of 60 and 70.

While it may not be necessary to remove every fibroid tumor in every case, it seems that in view of the malignant complications alone, putting aside the many other evil effects of these growths, it is dangerous to treat these tumors conservatively in patients more than 40 years of age.

Those adhering to the classical teaching assert that the tumors should be kept under observation until symptoms of malignancy or other dangers arise.

This is contrary to the surgical teaching of the age, which is essentially one of prevention of grave dangers by exposure to the lesser danger of operative cure.

Were there distinctive symptoms by which the advent of malignancy in cases of fibroid tumors could be recognized, the dangers of conservative and expectant treatment might be less.; but who can say when a fibroid has become sarcomatous or how long a cancer will be confined to the uterus? Sarcoma often occurs without increase in growth of a fibroid and adenocarcinoma may cause but little additional discharge or hemorrhage in a case of fibroids which has excessive menstruation or bleeding.

Those advising against operation in fibroid tumors in women over 40 years should remember that fibroid tumors are always dangerous, and that the older the patient is the more dangers these growths have. The menopause, instead of bringing a cure to fibroids, is but the precursor of more dangerous complications. The smouldering fire should not be watched until the house is in flames.

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